

Features	p-value	Persistent mean	Recent mean	Description	Dynamics in time	Interpretation
1. Mean distance	1.41E-24	0.034	0.015	Average number of point mutations between pairs of haplotypes. Measures diversity	↑	Accumulation of mutations and diversification over the course of intra-host evolution
2. Std distance	4.10E-14	0.019	0.010	Standard deviation of number of point mutations between pairs of haplotypes. Measures diversity.	↑	
3. Conservation score	5.11E-25	0.422	0.188	Average distance between the observed nucleotides and their consensuses. The distance is based on the NUC44 scoring matrix. Measures diversity	↑	
4. Mutation frequency	3.07E-16	0.023	0.010	Average number of point mutations between haplotypes and the most frequent haplotype. Measures diversity.	↑	
5. k-entropy $E_k(k=10)$	7.00E-23	0.630	0.357	Average entropy of k -mers	↑	

				(subsequences of length k) starting at fixed genomic positions. Measures diversity.		
6. Frequency entropy E_L	4.56E-06	0.668	0.567	Entropy of observed haplotype frequencies. Measures diversity.	↑	
7. SNV entropy E_1	1.14E-21	0.084	0.043	Average entropy of SNV frequencies. Measures diversity.	↑	
8. Transversion mutation	1.06E-07	0.061	0.032	Frequency of mutations between purine and pyrimidine nucleotides.	↑	The role of genetic saturation
9. DN/DS	5.39E-10	0.713	1.330	Ratio of non-synonymous (DN) and synonymous (DS) substitutions. Measures the strength of selection	↓	Increase in purifying selection indicating a growing role of intra-host adaptation
10. PCA complexity	1.4E-03	0.0053	0.0125	Percentage of principal components required to explain at least $\alpha=50\%$ percent of the observed genetic variance. Measures the	↓	Increase of structuredness of intra-host viral populations, possibly associated with intra-host adaptation and

				population complexity.		emergence of specialization
11. Kolmogorov complexity	1.55E-11	0.041	0.052	The highest possible degree of compression of observed viral sequences without loss of information. Measures the population complexity.	↓	
12. Robustness/Selection balance	3.66E-15	0.628	0.386	Correlation between haplotype frequencies and haplotype centralities in the observed genetic network. Measures the balance between mutational robustness and selection.	↑	
13. s-metric	1.93E-20	0.001	0.044	Network theory feature that measures how close a genetic network is to being scale-free (a type of networks characterized by the presence of hubs, small diameter and a power-law degree distribution)	↓	The major role of multiple founders at the earlier infection stage, later superseded by the increased role of mutational robustness.

14. Clustering coefficient	2·08E-13	0·082	0·356	Network theory feature that measures the propensity of haplotypes to cluster together in the genetic network	↓	
15. ODE feature C_{ODE}	2·42E-06	-0·270	0·224	The estimation of a population age using a dynamic model of viral evolution under the immune system's pressure.	N/A	Declining role of immune escape
16. Biochemical feature	2·92E-35	0·628	0·379	Total frequency of haplotypes identified as having a physico- chemical profile pointing to persistent infection.	↑	The change of physico- chemical properties is likely to be associated with transition between evolutionary mechanisms responsible for virus survival and proliferation at different infection stages.

Table S1: Descriptions and statistical results for analyzed features.